

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1-47. (Withdrawn)

48. (Currently Amended) An isolated nucleic acid, comprising a sequence of beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 43 or a perfect complementary sequence of any of such nucleotides.

49-50. (Canceled)

51. (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 48 and a promoter, wherein the nucleic acid and the promoter are operably linked.

52. (Original) The recombinant expression vector of claim 51, wherein said vector is suitable for transfection of a bacterial cell.

53. (Original) A heterologous cell transfected with the vector of claim 51, wherein said cell expresses a biologically active  $\beta$ -secretase.

54. (Original) The cell of claim 53, wherein said cell is a eukaryotic cell.

55. (Original) The cell of claim 53, wherein said cell is a bacterial cell.

56. (Original) The cell of claim 53, wherein said cell is an insect cell.

57. (Original) The cell of claim 53, wherein said cell is a yeast cell.

58. (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of

nucleotides that encodes SEQ ID NO: 43 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

59. (Original) The method of claim 58, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

60. (Previously Amended) The method of claim 59, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

61. (Original) The method of claim 58, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

62. (Previously Presented) The method of claim 61, wherein said antibody binds specifically to SEQ ID NO: 43.

63. (Previously Amended) The method of claim 61, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

64. (Previously Presented) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 43 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

65. (Original)) The cell of claim 64, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

66. (Previously Amended) The cell of claim 64, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

67. (Original) The cell of claim 64, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

68. (Previously Amended) The cell of claim 64, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

69. (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 82.

70-113. (Canceled)

114. (Currently Amended) An isolated nucleic acid, comprising a sequence of beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 58 or a perfect complementary sequence of any of such nucleotides.

115. (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 114 and a promoter, wherein the nucleic acid and the promoter are operably linked.

116. (Previously Presented) The expression vector of claim 115, wherein said vector is suitable for transfection of a bacterial cell.

117. (Previously Presented) A heterologous cell transfected with the vector of claim 115, wherein said cell expresses a biologically active  $\beta$ -secretase.

118. (Previously Presented) The cell of claim 117, wherein said cell is a eukaryotic cell.

119. (Previously Presented) The cell of claim 117, wherein said cell is a bacterial cell.

120. (Previously Presented) The cell of claim 117, wherein said cell is an insect cell.

121. (Previously Presented) The cell of claim 117, wherein said cell is a yeast cell.

122. (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 59 or a perfect complementary sequence of any of such nucleotides.

123. (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 122 and a promoter, wherein the nucleic acid and the promoter are operably linked.

124. (Previously Presented) The expression vector of claim 123, wherein said vector is suitable for transfection of a bacterial cell.

~~125,126-~~ (Previously Presented) A heterologous cell transfected with the vector of claim 123, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~126,127-~~ (Previously Presented) The cell of claim 125, claim 126, wherein said cell is a eukaryotic cell.

~~127,128-~~ (Previously Presented) The cell of claim claim 125, claim 126, wherein said cell is a bacterial cell.

~~128,129-~~ (Previously Presented) The cell of claim 125, claim 126, wherein said cell is an insect cell.

~~129.130.~~ (Previously Presented) The cell of claim 125, ~~claim 126~~, wherein said cell is a yeast cell.

~~130.131.~~ (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 66 or a perfect complementary sequence of any of such nucleotides.

~~131.132.~~ (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 130, ~~claim 131~~ and a promoter, wherein the nucleic acid and the promoter are operably linked.

~~132.133.~~ (Previously Presented) The expression vector of claim 131, ~~claim 132~~, wherein said vector is suitable for transfection of a bacterial cell.

~~133.134.~~ (Previously Presented) A heterologous cell transfected with the vector of claim 130, ~~claim 131~~, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~134.135~~ (Previously Presented) The cell of claim 133, ~~claim 134~~, wherein said cell is a eukaryotic cell.

~~135.136.~~ (Previously Presented) The cell of claim 133, ~~claim 134~~, wherein said cell is a bacterial cell.

~~136.137.~~ (Previously Presented) The cell of claim 133, ~~claim 134~~, wherein said cell is an insect cell.

~~137.138.~~ (Previously Presented) The cell of claim 133, ~~claim 134~~, wherein said cell is a yeast cell.

~~138.139.~~ (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 67 or a perfect complementary sequence of any of such nucleotides.

~~139.140.~~ (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 138~~claim 139~~ and a promoter, wherein the nucleic acid and the promoter are operably linked.

~~140.141.~~ (Previously Presented) The expression vector of claim 139~~claim 140~~, wherein said vector is suitable for transfection of a bacterial cell.

~~141.142.~~ (Previously Presented) A heterologous cell transfected with the vector of claim 139~~claim 140~~, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~142.143.~~ (Previously Presented) The cell of claim 141~~claim 142~~, wherein said cell is a eukaryotic cell.

~~143.144.~~ (Previously Presented) The cell of claim 141~~claim 142~~, wherein said cell is a bacterial cell.

~~144.145.~~ (Previously Presented) The cell of claim 141~~claim 142~~, wherein said cell is an insect cell.

~~145.146.~~ (Previously Presented) The cell of claim 141~~claim 142~~, wherein said cell is a yeast cell.

~~146.147.~~ (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 68 or a perfect complementary sequence of any of such nucleotides.

~~147.148.~~ (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 146~~claim 147~~, and a promoter, wherein the nucleic acid and the promoter are operably linked.

~~148.149.~~ (Previously Presented) The expression vector of claim 147~~claim 148~~, wherein said vector is suitable for transfection of a bacterial cell.

~~150.150.~~ (Previously Presented) A heterologous cell transfected with the vector of claim 147~~claim 148~~, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~150.151.~~ (Previously Presented) The cell of claim 149, ~~claim 150~~, wherein said cell is a eukaryotic cell.

~~151.152.~~ (Previously Presented) The cell of claim 149, ~~claim 150~~, wherein said cell is a bacterial cell.

~~152.153.~~ (Previously Presented) The cell of claim 149, ~~claim 150~~, wherein said cell is an insect cell.

~~153.154.~~ (Previously Presented) The cell of claim 149, ~~claim 150~~, wherein said cell is a yeast cell.

~~154.155.~~ (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 69 or a perfect complementary sequence of any of such nucleotides.

~~155.156.~~ (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 154, ~~claim 155~~, and a promoter, wherein the nucleic acid and the promoter are operably linked.

~~156.157.~~ (Previously Presented) The expression vector of claim 155, ~~claim 156~~, wherein said vector is suitable for transfection of a bacterial cell.

~~157.158.~~ (Previously Presented) A heterologous cell transfected with the vector of claim 155, ~~claim 156~~, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~158.159.~~ (Previously Presented) The cell of claim 157, ~~claim 158~~, wherein said cell is a eukaryotic cell.

~~159.160.~~ (Previously Presented) The cell of claim 157, ~~claim 158~~, wherein said cell is a bacterial cell.

~~160.161.~~ (Previously Presented) The cell of claim 157, ~~claim 158~~, wherein said cell is an insect cell.

~~161.162.~~ (Previously Presented) The cell of claim 157,~~claim 158~~, wherein said cell is a yeast cell.

~~162.163.~~ (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 70 or a perfect complementary sequence of any of such nucleotides.

~~163.164.~~ (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 162,~~claim 163~~, and a promoter, wherein the nucleic acid and the promoter are operably linked.

~~164.165.~~ (Previously Presented) The expression vector of claim 162,~~claim 163~~, wherein said vector is suitable for transfection of a bacterial cell.

~~165.166.~~ (Previously Presented) A heterologous cell transfected with the vector of claim 163,~~claim 164~~, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~166.167.~~ (Previously Presented) The cell of claim 165,~~claim 166~~, wherein said cell is a eukaryotic cell.

~~167.168.~~ (Previously Presented) The cell of claim 165,~~claim 166~~, wherein said cell is a bacterial cell.

~~168.169.~~ (Previously Presented) The cell of claim 165,~~claim 166~~, wherein said cell is an insect cell.

~~169.170.~~ (Previously Presented) The cell of claim 165,~~claim 166~~, wherein said cell is a yeast cell.

~~170.171.~~ (Currently Amended) An isolated nucleic acid, comprising a sequence beta-secretase encoding nucleotides, the beta-secretase encoding nucleotides consisting of nucleotides encoding nucleotides that encodes SEQ ID NO: 74 or a perfect complementary sequence of any of such nucleotides



~~171.172.~~ (Previously Presented) An expression vector, comprising the isolated nucleic acid of claim 170, ~~claim 171~~, and a promoter, wherein the nucleic acid and the promoter are operably linked.

~~172.173.~~ (Previously Presented) The expression vector of claim 171, ~~claim 172~~, wherein said vector is suitable for transfection of a bacterial cell.

~~173.174.~~ (Previously Presented) A heterologous cell transfected with the vector of claim 171, ~~claim 172~~, wherein said cell expresses a biologically active  $\beta$ -secretase.

~~174.175.~~ (Previously Presented) The cell of claim 173, ~~claim 174~~, wherein said cell is a eukaryotic cell.

~~175.176.~~ (Previously Presented) The cell of claim 173, ~~claim 174~~, wherein said cell is a bacterial cell.

~~176.177.~~ (Previously Presented) The cell of claim 173, ~~claim 174~~, wherein said cell is an insect cell.

~~177.178.~~ (Previously Presented) The cell of claim 173, ~~claim 174~~, wherein said cell is a yeast cell.

~~178.179.~~ (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 58 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

~~179.180.~~ (Previously Presented) The method of claim 178, ~~claim 179~~, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

~~180.181.~~ (Previously Amended) The method of claim 179, ~~claim 180~~, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

~~181.182.~~ (Previously Presented) The method of claim 178,~~claim 179~~, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

~~182.183.~~ (Previously Presented) The method of claim 181,~~claim 182~~, wherein said antibody binds specifically to SEQ ID NO: 58.

~~183.184.~~ (Previously Presented) The method of claim 181,~~claim 182~~, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

~~184.185.~~ (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 59 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

~~185.186.~~ (Previously Presented) The method of claim 184,~~claim 185~~, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

~~186.187.~~ (Previously Presented) The method of claim 185,~~claim 186~~, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

~~187.188.~~ (Previously Presented) The method of claim 184,~~claim 185~~, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

~~188.189.~~ (Previously Presented) The method of claim 187,~~claim 188~~, wherein said antibody binds specifically to SEQ ID NO: 59.

~~189.190.~~ (Previously Presented) The method of claim 187,~~claim 188~~, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

190.191. (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 66 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

191.192. (Previously Presented) The method of claim 190, claim 191, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

192.193. (Previously Presented) The method of claim 191, claim 192, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

193.194 (Previously Presented) The method of claim 190, claim 191, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

194.195. (Previously Presented) The method of claim 193, claim 194, wherein said antibody binds specifically to SEQ ID NO: 66.

195.196. (Previously Presented) The method of claim 193, claim 194, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

196.197. (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 67 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

197.198. (Previously Presented) The method of claim 196, claim 197, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

~~198.199.~~ (Previously Presented) The method of claim 197,~~claim 198~~, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

~~199.200.~~ (Previously Presented) The method of claim 196,~~claim 197~~, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

~~200.201.~~ (Previously Presented) The method of claim 199,~~claim 200~~, wherein said antibody binds specifically to SEQ ID NO: 67.

~~201.202.~~ (Previously Presented) The method of claim 196,~~claim 197~~, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

~~202.203.~~ (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 68 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

~~203.204.~~ (Previously Presented) The method of claim 202,~~claim 203~~, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

~~204.205.~~ (Previously Presented) The method of claim 203,~~claim 204~~, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

~~205.206.~~ (Previously Presented) The method of claim 202,~~claim 203~~, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

~~206.207.~~ (Previously Presented) The method of claim 205,~~claim 206~~, wherein said antibody binds specifically to SEQ ID NO: 68.

207.208. (Previously Presented) The method of claim 205,claim-206, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

208.209. (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 69 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

209.210. (Previously Presented) The method of claim 208,claim-209, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

210.211. (Previously Presented) The method of claim 209,claim-210, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

211.212. (Previously Presented) The method of claim 210,claim-211, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

212.213. (Previously Presented) The method of claim 208,claim-209, wherein said antibody binds specifically to SEQ ID NO: 69.

213.214. (Previously Presented) The method of claim 211,claim-212, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

214.215. (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 70 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

~~215.216.~~ (Previously Presented) The method of claim 214,~~claim 215~~, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

~~216.217.~~ (Previously Presented) The method of claim 215,~~claim 216~~, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

~~217.218.~~ (Previously Presented) The method of claim 214,~~claim 215~~, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

~~218.219.~~ (Previously Presented) The method of claim 217,~~claim 218~~, wherein said antibody binds specifically to SEQ ID NO: 70.

~~219.220.~~ (Previously Presented) The method of claim 217,~~claim 218~~, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

~~220.221.~~ (Previously Presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 74 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

~~221.222.~~ (Previously Presented) The method of claim 220,~~claim 221~~, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

~~222.223.~~ (Previously Presented) The method of claim 221,~~claim 222~~, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

~~223.224.~~ (Previously Presented) The method of claim 220,~~claim 221~~, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

~~224.225.~~ (Previously Presented) The method of claim 223,~~claim 224~~, wherein said antibody binds specifically to SEQ ID NO: 74.

~~225.226.~~ (Previously Presented) The method of claim 220, ~~claim 221~~, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

~~226.227.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

~~227.228.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

~~228.229.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

~~229.230.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

~~230.231.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

~~231.232.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

~~232.233.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~233.234.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~234.235.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

~~235.236.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~236.237.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~237.238.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~238.239.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~239.240.~~ (Previously Presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~240.241.~~ (Previously Presented) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 58 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

~~241.242.~~ (Previously Presented) The cell of ~~claim 240, claim 241,~~ wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

~~242.243.~~ (Previously Presented) The cell of ~~claim 240, claim 241,~~ wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

~~243.244.~~ (Previously Presented) The cell of ~~claim 240, claim 241,~~ wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

~~244.245.~~ (Previously Presented) The cell of ~~claim 240, claim 241,~~ wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-



terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

245.246. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

246.247. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

247.248. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

248.249. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

249.250. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

250.251. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

251.252. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

252.253. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

253.254. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

254.255. (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~255.256.~~ (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~256.257.~~ (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~257.258.~~ (Previously Presented) The cell claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~258.259.~~ (Previously Presented) The cell of claim 243, ~~claim 244~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~259.260~~ (Previously Presented) A heterologous cell, comprising

- (i) a nucleic acid molecule encoding SEQ ID NO: 59 or the complementary sequence of said nucleic acid molecule;
- (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
- (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

~~260.261.~~ (Previously Presented) The cell of claim 259, ~~claim 260~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

~~261.262.~~ (Previously Presented) The cell of claim 259, ~~claim 260~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

~~262.263.~~ (Previously Presented) The cell of claim 259, ~~claim 260~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

~~263.264.~~ (Previously Presented) The cell of claim 259,~~claim 260~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

~~264.265.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

~~265.266.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

~~268.267.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

~~267.268.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

~~268.269.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

~~269.270.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

~~270.271.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~271.272.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~272.273.~~ (Previously Presented) The cell of claim 262,~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

273.274. (Previously Presented) The cell of claim 262, ~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

274.275. (Previously Presented) The cell of claim 262, ~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

275.276. (Previously Presented) The cell of claim 262, ~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

276.277. (Previously Presented) The cell of claim 262, ~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

277.278. (Previously Presented) The cell of claim 262, ~~claim 263~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

278.279. (Previously Presented) A heterologous cell, comprising

- (i) a nucleic acid molecule encoding SEQ ID NO: 66 or the complementary sequence of said nucleic acid molecule;
- (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
- (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

279.280. (Previously Presented) The cell of claim 278, ~~claim 279~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

280.281. (Previously Presented) The cell of claim 278, ~~claim 279~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

281.282. (Previously Presented) The cell of claim 278, ~~claim 279~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

282.283. (Previously Presented) The cell of claim 278, ~~claim 279~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

283.284. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

284.285. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

285.286. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

286.287. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

287.288. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

288.289. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

289.290. (Previously Presented) The cell of claim 281, ~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~290.291.~~ (Previously Presented) The cell of claim 281,~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~291.292.~~ (Previously Presented) The cell of claim 281,~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

~~292.293.~~ (Previously Presented) The cell of claim 281,~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~293.294.~~ (Previously Presented) The cell of claim 281,~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~294.295.~~ (Previously Presented) The cell of claim 281,~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~295.296.~~ (Previously Presented) The cell of claim 281,~~claim 282~~ wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~296.297.~~ (Previously Presented) The cell of claim 281,~~claim 282~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~297.298.~~ (Previously Presented) A heterologous cell, comprising

- (i) a nucleic acid molecule encoding SEQ ID NO: 67 or the complementary sequence of said nucleic acid molecule;
- (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
- (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

~~298.299.~~ (Previously Presented) The cell of claim 297,~~claim 298~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

~~299.300.~~ (Previously Presented) The cell of claim 297,~~claim 298~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

~~300.301.~~ (Previously Presented) The cell of claim 297,~~claim 298~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

~~301.302.~~ (Previously Presented) The cell of claim 297,~~claim 298~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

~~302.303.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

~~303.304.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

~~304.305.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

~~305.306.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

~~306.307.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

~~307.308.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

~~308.309.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~309.310.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~310.311.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

~~311.312.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~312.313.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~311.312.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~312.313.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~313.314.~~ (Previously Presented) The cell of claim 300,~~claim 301~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~314.315.~~ (Previously Presented) A heterologous cell, comprising

- (i) a nucleic acid molecule encoding SEQ ID NO: 68 or the complementary sequence of said nucleic acid molecule;
- (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and
- (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.



315.316. (Previously Presented) The cell of claim 314, ~~claim 315~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

316.317. (Previously Presented) The cell of claim 314, ~~claim 315~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

317.318. (Previously Presented) The cell of claim 314, ~~claim 315~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

318.319. (Previously Presented) The cell of claim 314, ~~claim 315~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

319.320. (Previously Presented) The cell of claim 317, ~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

320.321. (Previously Presented) The cell of claim 317, ~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

321.322. (Previously Presented) The cell of claim 317, ~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

322.323. (Previously Presented) The cell of claim 317, ~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

323.324. (Previously Presented) The cell of claim 317, ~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

~~324.325.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

~~325.326.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~326.327.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~327.328.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

~~328.329.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~329.330.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~330.331.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~331.332.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~332.333.~~ (Previously Presented) The cell of claim 317,~~claim 318~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~333.334.~~ (Previously Presented) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 69 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

~~334.335.~~ (Previously Presented) The cell of claim 333, ~~claim 334~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

~~335.336.~~ (Previously Presented) The cell of claim 333, ~~claim 334~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

~~336.337.~~ (Previously Presented) The cell of claim 333, ~~claim 334~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

~~337.338.~~ (Previously Presented) The cell of claim 333, ~~claim 334~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

~~338.339.~~ (Previously Presented) The cell of claim 336, ~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

~~339.340.~~ (Previously Presented) The cell of claim 336, ~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

~~340.341.~~ (Previously Presented) The cell of claim 336, ~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

~~341.342.~~ (Previously Presented) The cell of claim 336, ~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

~~342.343.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

~~343.344.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

~~344.345.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~345.346.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~346.347.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

~~347.348.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~348.349.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~349.350.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~350.351.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~351.352.~~ (Previously Presented) The cell of claim 336,~~claim 337~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~352.353.~~ (Previously Presented) A heterologous cell, comprising  
(i) a nucleic acid molecule encoding SEQ ID NO: 70 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

~~353.354.~~ (Previously Presented) The cell of claim 352,~~claim 353~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

~~354.355.~~ (Previously Presented) The cell of claim 352,~~claim 353~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

~~355.356.~~ (Previously Presented) The cell of claim 352,~~claim 353~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

~~356.357.~~ (Previously Presented) The cell of claim 352,~~claim 353~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

~~357.358.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

~~358.359.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

~~359.360.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

~~360.361.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

~~361.362.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

~~362.363.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

~~363.364.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

~~364.365.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

~~365.366.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

~~366.367.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

~~367.368.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

~~368.369.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

~~369.370.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

~~370.371.~~ (Previously Presented) The cell of claim 355,~~claim 356~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

~~371.372.~~ (Previously Presented) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 74 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

~~372.373.~~ (Previously Presented) The cell of claim 371, ~~claim 372~~, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

~~373.374.~~ (Previously Presented) The cell of claim 371, ~~claim 372~~, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

~~374.375.~~ (Previously Presented) The cell of claim 371, ~~claim 372~~, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

~~375.376.~~ (Previously Presented) The cell of claim 371, ~~claim 372~~, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

~~376.377.~~ (Previously Presented) The cell of claim 374, ~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

~~377.378.~~ (Previously Presented) The cell of claim 374, ~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

378.379. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

379.380. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

380.381. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

381.383. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

382.383. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

383.384. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

384.385. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

385.386. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

386.387. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

387.388. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

388.389. (Previously Presented) The cell of claim 374,~~claim 375~~, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.



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Amendment dated September 1, 2005  
Reply to Office Action of March 1, 2005

~~389.390.~~ (Previously Presented) The cell of claim 374, ~~claim 375~~, wherein  
said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.